## REMARKS

In response to the Examiner's contention that nucleic or amino acid sequences appear in the specification on pages 85, 86, and 104 and in the Brief Description of Drawings of Figures 5A through to 5G, 6C, and 10, it is requested that the Sequence Listing in written and computer readable form from prior application no. 08/639,255, filed on April 24, 1996 be made a part of the present application as provided for by 37 C.F.R. §1.821(e). Pursuant to 37 C.F.R. §1.821(f), a statement regarding the identity of sequences disclosed in the specification and the content of the written and computer readable copies of the Sequence Listing is submitted concurrently herewith. The specification has been amended to incorporate the sequence identifiers pursuant to 37 C.F.R. § 1.821(d). The above-made amendments do not constitute new matter under 35 U.S.C. § 132.

Claims 27-50 are pending in this application.

## The Rejection Under 35 U.S.C. § 112 Is Improper

Claims 34, 35, 41, 42, 45, 47, 49, and 50 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleges that the specification does not provide written support for probes of biosynthetic genes for: mevalonic acid, glucose transfer systems, beta lactams, macrolides, alkaloids, bryostatins, carotenoids, steroids, retinoids, tetracycline, oxytetracycline, puromycin, doxorubicin, taxol, chloramphenicol, nalidixic acid, mithramycin, novobiocin, vulpinic acid, usnic acid, kainic

acid, podophyllotoxin, brevitoxin, camptothecin, or artemisinin. Applicants respectfully disagree.

According to the case law, in order to provide an adequate written description, the specification must reasonably convey to the artisan that the inventor had possession at that time of the claimed subject matter. While a patent applicant does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art to recognize that the applicant invented what is claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991) (citing *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989)). "The written description must communicate that which is needed to enable the skilled artisan to make and use the claimed invention." *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419, 1421, 5 U.S.P.Q.2d 1194, 1197 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1998).

In this instance, the specification teaches the construction of a biased combinatorial library by pre-screening with probes from "any cloned biosynthetic pathway" (page 63, line 35) and provides "polyketide biosynthetic loci" as an example because they are the best characterized biosynthetic loci. The specification further states that the principles governing the creation of such libraries "may be applied to other antibiotic or secondary metabolite biosynthetic loci" (page 64, lines 5-6) and noted that "Other cloned biosynthetic pathway, such as peptide synthases and aminoglycoside synthases, can also provide probes for pre-screening the initial libraries." (page 64, lines 14-16). In view of the foregoing, Applicants submit that the specification clearly described different kinds of probes for genes responsible for the biosynthesis of other compounds, including those compounds which have been particularly mentioned in the specification. For example, alkaloids, bryostatins, carotenoids, steroids, retinoids, taxol, vulpinic acid, usnic acid, kainic acid, podophyllotoxin,

brevitoxin, camptothecin, and artemisinin are mentioned in the specification in Table II on pages 29-30, wherein it is taught that these compounds are produced by donor organisms used to provide genetic material for the creation of the claimed combinatorial gene expression libraries. In particular, the specification describes that genes encoding enzymes for the biosynthesis of carotenoids (such as zeaxanthin and beta-crytoxanthin), as well as genes encoding glucose transfer systems are cloned and characterized (page 53, lines 11-22); and that marinone, a natural product made by marine microbes, is a product of mixed polyketide and mevalonic acid biosynthetic pathway (page 25, l18-24). Oxytetracycline is mentioned in section 5.1.6 entitled "Biased combinatorial gene expression libraries" on page 63, line 23.

Furthermore, beta lactams, macrolides, puromycin, doxorubicin, taxol, chloramphenicol, nalidixic acid, mithramycin, and novobiocin are mentioned in the specification in Table III on page 49. The specification teaches that efflux systems for these compounds are useful for incorporation into a host organism such that when these compounds are produced in large quantities in library cells, they are secreted and do not accumulate to toxic levels inside the cells. "When the libraries are used for the purpose of generating secondary metabolites, the toxicity of the compounds can lead to under-representation of these productive host organisms in the library." (page 47, lines 19-23). All the compounds recited in the rejected claims have been described in the specification in connection with the preparation of a combinatorial gene expression library. Applicants submit that the support is provided inherently in the disclosure of the biosynthesis of the compounds and the methods of making a biased combinatorial gene expression library. Applicants further submit that the genes for biosynthesis of the recited compounds are known, for example, Wildrung et al. "A

cDNA clone for taxdiene synthase, the diterpene cyclase that catalyzes the committed step of taxol biosynthesis", J. Biol. Chem. 271:920-4 (Apr 19, 1996).

Applicants respectfully point out that many of the compounds recited in the rejected claims belong to the groups of compounds recited in the non-rejected claims, for example, doxorubicin, mithramycin, tetracyclines and oxytetracyclines are polyketide compounds; and that beta lactams (such as penicillin), macrolides (such as erythromycin), puromycin, doxorubicin, chloramphenicol, mithramycin, novobiocin vulpinic acid, and usnic acid, are antibiotics.

According to applicable case law, "ipsis verbis disclosure is not necessary to satisfy the written description requirement of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question." Fujikawa v. Wattanasin, 93 F.3d 1559, 39 U.S.P.Q. 2d 1895, 1904 (Fed. Cir. 1996). In this instance, the specification has conveyed to the skilled artisan the compounds of interest as recited, and the probes and methods for making the libraries that produce these compounds within the meaning of 35 U.S.C. § 112 first paragraph. Applicants respectfully submits that the disclosure reflects that the inventor had possession of the claimed subject matter and communicates that which is needed to enable the skilled artisan to make and use the invention.

In view of the foregoing, the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

**The Rejection Under 35 U.S.C. § 102 Is Obviated**

Claims 27-34, 36-41, 43-46, and 48-50 are rejected under 35 U.S.C. § 102(f) because allegedly, Applicants did not invent the claimed subject matter.

The Examiner alleges that U.S. Patent No. 5,824,485 (the '485 patent) discloses a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms; and provides guidance to isolate donor organisms from an environmental sample (e.g., soil, deposits near hot springs or thermal vents, freshwater or seawater filtrates, or marine or estuarine sediments), to make selected libraries that encode proteins that are involved in secondary metabolism, and to use vectors for introduction of the library into host cells. As such, the Examiner alleges that the '485 patent anticipates the claimed invention of this application because the inventive entities for both are different.

The present application is a divisional application of application 08/783,944 (now U.S. Patent No. 5,783,431), which is a continuation-in-part of application no. 08/639,255 (now U.S. Patent No. 5,824,485). The inventive entity of U.S. Patent No. 5,824,485 was Katie A. Thompson, Lyndon M. Foster, Todd C. Peterson, Nicole M. Nasby, and Paul Brian. The inventive entity of this application differs by the absence of Katie A. Thompson and Nicole M. Nasby as coinventors.

Applicants respectfully submit that the preliminary amendment of the claims filed in the present application on June 2, 1999 resulted in the inclusion in the pending claims of subject matters that was co-invented by Katie A. Thompson. The subject matters covered by the currently pending claims were disclosed but not originally claimed when the application was filed on December 5, 1997. Accordingly, Applicants submit herewith a

Petition to Correct Inventorship Pursuant to 37 C.F.R. § 1.48(c) and supporting documents to remedy the omission of Katie A. Thompson as a coinventor. Thus, the inventive subject matter in question which is disclosed and claimed in the instant application is attributable to coinventors Todd C. Peterson, Lyndon M. Foster, Paul Brian, and Katie A. Thompson only.

The other coinventor of the '485 patent, Nicole M. Nasby, did not contribute to the invention of the presently claimed subject matter. Nicole M. Nasby contributed to the invention that relates to methods that involve encapsulating the host organisms containing a combinatorial gene expression library in a semi-solid matrix to facilitate high-throughput drug screening processes. Such methods are not claimed in the present application.

Upon the addition of Katie A. Thompson as a coinventor of this application, Applicants submit that all of the inventors of the claimed subject matter are properly identified and therefore, the rejection under 35 U.S.C. § 102(f) should be withdrawn.

**The Obviousness-Type Double Patenting Rejection Is Obviated**

Claims 27-29, 32-36, 39-42, and 44-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21 and 22 of U.S. Patent No. 5,783,431 (the '431 patent) in view of Vinning (*Gene*, 1992, 155:135-140). The Examiner contends that it would have been obvious to use the method of library construction of claims 21 and 22 of the '431 patent to select for sequences that encode proteins involved in secondary metabolism, because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

Claims 27-29, 32-36, and 39-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 8, and 10 of U.S. Patent No. 5,824,485 in view of Vining. The Examiner alleges that it would have been obvious to modify the library of claims 3, 8, and 10 of the '485 patent by adding the step of selecting for sequences that encode proteins involved in secondary metabolism, because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

The Examiner further alleges that while the conflicting claims in the '431 and '485 patents are not identical to the rejected claims, they are not patentably distinct.

In response, while not admitting that claims 27-29, 32-36, 39-42, and 44-49 of the above-identified patent application are not patentably distinct from claims 21 and 22 of the '431 patent and claims 3, 8, and 10 of the '485 patent, Applicants submit herewith a Terminal Disclaimer under 37 C.F.R. § 1.321(b) executed by Mario Thomas, President and Chief Executive Officer of TerraGen Discovery Inc., the assignee of the above-identified application (1) disclaiming any part of claims 27-29, 32-36, 39-42, and 44-49 of any patent granted on the present application (Serial No. 08/986,186) which could extend beyond the expiration date of U.S. Patent Nos. 5,783,431 or 5,824,485; and (2) ensuring that any such patent granted on the present application shall be enforceable only for and during such period that such patent is commonly owned with U.S. Patent No. 5,783,431 or 5,824,485.

By this terminal disclaimer, and as stated therein, the assignee does not disclaim any terminal part of any patent granted on application Serial No. 08/986,186 prior to the expiration date of the full statutory term of U.S. Patent No. 5,783,431 and 5,824,485, as presently shortened by any terminal disclaimer, in the event that U.S. Patent No. 5,783,431 and 5,824,485 later expire for failure to pay a maintenance fee, are held unenforceable, are

found invalid by a court of competent jurisdiction, are statutorily disclaimed in whole or terminally disclaimed under 37 C.F.R. § 1.321, have all claims canceled by a reexamination certificate, or are otherwise terminated prior to the expiration of its statutory term as presently shortened by any terminal disclaimer, except for the separation of legal title stated above.

Applicants assert that the submission of the Terminal Disclaimer obviates the rejection because Vinning alone does not suggest the Applicants' invention. Applicants respectfully request the withdrawal of the obviousness-type double patenting rejection.

## CONCLUSION

Applicants respectfully request that the foregoing amendments and remarks be entered and made of record in the file history of the application. The claims are believed to be patentable and free of the art. Early allowance is respectfully requested.

Respectfully submitted,

Laura A. Coruzzi By: [signature] 40,258

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Enclosures